

**IN THE CLAIMS:**

Please cancel claims 2 through 42.

**MARKED UP VERSION OF PENDING CLAIMS**

1. A method of removing a pathogen from a mixture containing a compound and the pathogen, the method comprising:
  - (a) placing the compound and pathogen in a first solvent stream, the first solvent stream being separated from a second solvent stream by a selective membrane having a defined pore size;
  - (b) selecting a buffer for the first solvent stream having a required pH;
  - (c) applying an electric potential across the first and second solvent streams, wherein the application of such electric potential causes movement of at least a portion of the compound through the membrane into the second solvent stream while the pathogen is substantially retained in the first solvent stream, or if entering the membrane, being substantially prevented from entering the second solvent stream and wherein substantially all transmembrane migration of the compound is initiated by application of the electric potential;
  - (d) optionally, periodically stopping and reversing the electric potential to cause the movement of any pathogens having entered the membrane to move back into the first solvent stream, wherein substantially not causing any compounds that have entered the second solvent stream to re-enter the first solvent stream; and
  - (e) maintaining step (c), and optional step (d) if used, until the second solvent stream contains the desired purity of the compound.
  
2. (Canceled) A method of removing a pathogen from a mixture containing a compound and pathogen, the method comprising:
  - (a) placing the compound and the pathogen in a first solvent stream, the first solvent stream being separated from a second solvent stream by a selective membrane having a defined pore size;

- (b) selecting a buffer for the first solvent stream having a required pH;
  - (c) applying an electric potential across the first and second solvent streams, wherein the application of such electric potential causes movement of at least a portion of the pathogen through the membrane into the second solvent stream while the compound is substantially retained in the first solvent stream, or if entering the membrane, being substantially prevented from entering the second solvent stream and wherein substantially all transmembrane migration of the pathogen is initiated by application of the electric potential;
  - (d) optionally, periodically stopping and reversing the electric potential to cause the movement of any compound having entered the membrane to move back into the first solvent stream, wherein substantially not causing any pathogens that have entered the second solvent stream to re-enter the first solvent stream; and
  - (e) maintaining step (c), and optional step (d) if used, until the first solvent stream contains the desired purity of the compound.
3. (Canceled) The method according to claim 1 wherein the compound is selected from the group consisting of blood proteins, immunoglobulins, recombinant proteins, and combinations thereof.
  4. (Canceled) The method according to claim 1 wherein the pathogen is selected from the group consisting of viruses, bacteria, prions, and combinations thereof.
  5. (Canceled) The method according to claim 1 wherein the pathogen is a virus.
  6. (Canceled) The method according to claim 1 wherein the pathogen is a bacterium.
  7. (Canceled) The method according to claim 1 wherein the pathogen is a prion.
  8. (Canceled) The method according to claim 1 or 2 wherein the biological contaminant is selected from the group consisting of lipopolysaccharide, toxin, and endotoxin.

9. (Canceled) The method according to claim 1 wherein the solvent for the first solvent stream has a pH lower than the isoelectric point of the compound.
10. (Canceled) The method according to claim 1 wherein the selective membrane has a molecular mass cut-off between about 3 and about 1000kDa.
11. (Canceled) The method according to claim 1 wherein the electric potential is up to 300 volts.
12. (Canceled) The method according to claim 1 or 2 wherein the biological contaminant is collected or removed from the first stream or second stream.
13. (Canceled) The method according to claim 1 wherein the selective membrane has a molecular mass cut-off close to the apparent molecular mass of the compound.
14. (Canceled) Use of Gradiflow in the purification or separation of biomolecule from a biological contaminant.
15. (Canceled) A compound and solvent stream substantially free from pathogens purified by the method according to claim 1.
16. (Canceled) Use of biomolecule according to claim 15 in medical and veterinary applications.
17. (Canceled) The method according to claim 1 wherein the solvent for the first solvent stream has a pH at about the isoelectric point of the compound.
18. (Canceled) The method according to claim 1 wherein the solvent for the first solvent stream has a pH above the isoelectric point of the compound.

19. (Canceled) The method according to claim 1 wherein the membrane has a molecular mass cut-off of at least about 3 kDa.
20. (Canceled) The method according to claim 1 wherein the compound is collected or removed from the second solvent stream.
21. (Canceled) The method according to claim 1 wherein step (e) results in the compound being substantially free of any pathogens.
22. (Canceled) The method according to claim 2 wherein the pathogen is selected from the group consisting of viruses, bacteria, prions, and combinations thereof.
23. (Canceled) The method according to claim 22 wherein the pathogen is a virus.
24. (Canceled) The method according to claim 22 wherein the pathogen is a bacterium.
25. (Canceled) The method according to claim 22 wherein the pathogen is a prion.
26. (Canceled) The method according to claim 2 wherein the compound is selected from the group consisting of blood proteins, immunoglobulins, recombinant proteins, and combinations thereof.
27. (Canceled) The method according to claim 2 wherein the solvent for the first solvent stream has a pH lower than the isoelectric point of the pathogen.
28. (Canceled) The method according to claim 2 wherein the solvent for the first solvent stream has a pH at about the isoelectric point of the pathogen.
29. (Canceled) The method according to claim 2 wherein the solvent for the first solvent stream has a pH above the isoelectric point of the pathogen.

30. (Canceled) The method according to claim 2 wherein the membrane has a molecular mass cut-off close to the apparent molecular mass of the pathogen.
31. (Canceled) The method according to claim 2 wherein the membrane has a molecular mass cut-off of at least about 3 kDa.
32. (Canceled) The method according to claim 31 wherein the membrane has a molecular mass cut-off of between 3 and 1000 kDa.
33. (Canceled) The method according to claim 2 wherein the electric potential applied is up to about 300 volts.
34. (Canceled) The method according to claim 2 wherein the pathogen is collected or removed from the second solvent stream.
35. (Canceled) The method according to claim 2 wherein substantially all of the pathogen is removed from the mixture.
36. (Canceled) The method according to claim 2 wherein the mixture comprises at least two types of pathogen and only one type is caused to move into the second solvent stream.
37. (Canceled) A compound and solvent stream substantially free from pathogens purified by the method according to claim 2.
38. (Canceled) The method according to claim 1 wherein the selective membrane has a molecular mass cut-off of at least about 3 kDa.
39. (Canceled) The method according to claim 1 further comprising the step of applying the electric potential across a third solvent stream, which third solvent stream is separated from a selected one of the first and second solvent streams by a second selective

membrane, so as to cause the migration of at least a portion of at least one of the compound and the pathogen through the second selective membrane and into the third solvent stream.

40. (Canceled) The method according to claim 39 further comprising the step of applying the electric potential across a fourth solvent stream, which fourth solvent stream is separated from the other of the first and second solvent streams by a third selective membrane, so as to cause the migration of at least a portion of at least one of the compound and the pathogen through the third selective membrane and into the fourth solvent stream.

41. (Canceled) The method according to claim 2 further comprising the step of applying the electric potential across a third solvent stream, which third solvent stream is separated from a selected one of the first and second solvent streams by a second selective membrane, so as to cause the migration of at least a portion of at least one of the compound and the pathogen through the second selective membrane and into the third solvent stream.

42. (Canceled) The method according to claim 41 further comprising the step of applying the electric potential across a fourth solvent stream, which fourth solvent stream is separated from the other of the first and second solvent streams by a third selective membrane, so as to cause the migration of at least a portion of at least one of the compound and the pathogen through the third selective membrane and into the fourth solvent stream.

43. (New) A method for concurrently isolating at least a portion of both a selected compound and biological contaminants from a fluid stream, the method comprising:

(a) directing a first fluid stream having a selected pH and including at least one biological contaminant and a selected compound so as to flow along a first selective membrane;

(b) directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby;

(c) directing a third fluid stream separated from one of the first and second fluid streams by a second selective membrane;

(d) applying at least one voltage potential across at least the first and second fluid streams, wherein the application of such at least one voltage potential causes movement of at least a portion of at least one of the selected compound and the biological contaminants through the first selective membrane into the second fluid stream, wherein the second selective membrane has a preselected pore size that allows selective migration of components in at least one of the first and second fluid streams through the second selective membrane into the third fluid stream; and

(e) maintaining step (d) until at least one of the fluid streams contains a desired purity of the selected compound.

44. (New) The method according to claim 43 wherein the first selective membrane has a preselected pore size so as to allow selective migration of components in the first fluid stream through the first selective membrane into the second fluid stream and selectively retain other components in the first fluid stream.

45. (New) The method according to claim 43 wherein the step of directing the third fluid stream comprises directing the third fluid stream so as to be separated from the second fluid stream by the second selective membrane.

46. (New) The method according to claim 45 wherein the second selective membrane has a preselected pore size so as to substantially prevent at least one of the selected compound and selected biological contaminants removed to the second fluid stream from migrating through the second selective membrane into the third fluid stream and substantially retain the at least one of the selected compound and selected biological contaminants in the second fluid stream.

47. (New) The method according to claim 46 wherein the application of a voltage potential across the third fluid stream causes movement of at least a portion of at least one of the selected compound and selected biological contaminants removed to the second fluid stream through the second selective membrane into the third fluid stream.

48. (New) The method according to claim 46 wherein the method further comprises directing a fourth fluid stream separated from the first fluid stream by a third selective membrane, wherein the preselected pore size of the third selective membrane allows selective migration of components in the first fluid stream through the third selective membrane into the fourth fluid stream.
49. (New) The method according to claim 48 wherein the third selective membrane has a preselected pore size so as to substantially prevent at least one of the any selected compound remaining in the first fluid stream, any biological contaminants remaining in the first fluid stream, and any other compounds remaining in the first fluid stream from migrating through the third selective membrane into the fourth fluid stream and substantially retain the at least one of the selected compound, biological contaminants, and other components in the second fluid stream.
50. (New) The method according to claim 48 wherein the application of a voltage potential across the fourth fluid stream causes migration of at least a portion of at least one of any selected compound remaining in the first fluid stream, any biological contaminants remaining in the first fluid stream, and any other compounds remaining in the first fluid stream through the third selective membrane into fourth fluid stream.
51. (New) The method according to claim 43 wherein the step of directing a third fluid stream directing the third fluid stream so as to be separated from the first fluid stream by the second selective membrane.
52. (New) The method according to claim 51 wherein the second selective membrane has a preselected pore size so as to substantially prevent at least one of the any selected compound remaining in the first fluid stream, any biological contaminants remaining in the first fluid stream, and any other compounds remaining in the first fluid stream from migrating through the second selective membrane into the third fluid stream and substantially retain at least one of the selected compound, biological contaminants, and other components in the first fluid stream.



53. (New) The method according to claim 51 wherein the application of a voltage potential across the third fluid stream causes migration of at least a portion of at least one of any selected compound remaining in the first fluid stream, any biological contaminants remaining in the first fluid stream, and any other compounds remaining in the first fluid stream through the second selective membrane into third fluid stream.

54. (New) The method according to claim 51 wherein the method further comprises directing a fourth fluid stream separated from the second fluid stream by a third selective membrane, wherein the preselected pore size of the third selective membrane allows selective migration of components in the second fluid stream through the third selective membrane into the fourth fluid stream.

55. (New) The method according to claim 54 wherein the third selective membrane has a preselected pore size so as to substantially prevent at least one of the selected compound and selected biological contaminants removed to the second fluid stream from migrating through the third selective membrane into the fourth fluid stream and substantially retain the at least one of the selected compound and selected biological contaminants in the second fluid stream.

56. (New) The method according to claim 54 wherein the application of a voltage potential across the fourth fluid stream causes movement of at least a portion of at least one of the selected compound and selected biological contaminants removed to the second fluid stream through the third selective membrane into the fourth fluid stream.

57. (New) The method according to claim 43 wherein the method further comprises periodically stopping and reversing the voltage potential to cause movement of at least any compounds of the first fluid stream having entered the first selective membrane to move back into the first fluid stream and wherein substantially not causing any of the selected compound and biological contaminants that have entered the second fluid stream to re-enter the first fluid stream.

58. (New) The method according to claim 43 wherein the first fluid stream further includes a compound from which the selected compound is separated, wherein such compound is selected from the group consisting of blood proteins, immunoglobulins, recombinant proteins, and combinations thereof.

59. (New) The method according to claim 43 wherein the biological contaminant is selected from the group consisting of viruses, bacteria, prions, yeast, lipopolysaccharides, toxins, endotoxins, and combinations thereof.

60. (New) The method according to claim 43 wherein the pH of the first fluid stream is selected by selectively adding a buffer having the required pH and the pH is selected at one of a pH lower than the isoelectric point of the compound, a pH about the isoelectric point of the compound, and a pH higher than the isoelectric point of the compound.

61. (New) A method for concurrently isolating at least a portion of both a selected compound and biological contaminants from a fluid stream, the method comprising:

- (a) directing a first fluid stream having a selected pH and including at least one biological contaminant and a selected compound so as to flow along a first selective membrane;
- (b) directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby;
- (c) directing a third fluid stream separated from one of the first and second fluid streams by a second selective membrane;
- (d) applying at least one voltage potential across at least the first and second fluid streams, wherein the application of such at least one voltage potential causes movement of at least a portion of the biological contaminants through the first selective membrane into the second fluid stream while the selected compound is prevented from entering the second fluid stream, wherein the second selective membrane has a preselected pore size that allows selective migration of components in at least one of the first and second fluid streams through the second selective membrane into the third fluid stream; and

(e) maintaining step (d) until at least one of the fluid streams contains a desired purity of the selected compound.

62. (New) The method according to claim 61 wherein the first selective membrane has a preselected pore size so as to allow selective migration of components in the first fluid stream through the first selective membrane into the second fluid stream and selectively retain other components in the first fluid stream.

63. (New) The method according to claim 61 wherein the step of directing the third fluid stream comprises directing the third fluid stream so as to be separated from the first fluid stream by the second selective membrane.

64. (New) The method according to claim 63 wherein the second selective membrane has a preselected pore size so as to substantially prevent at least one of the selected compound and selected biological contaminants remaining in the first fluid stream from migrating through the second selective membrane into the third fluid stream and substantially retain at least one of the selected compound and selected biological contaminants in the first fluid stream.

65. (New) The method according to claim 63 wherein the application of a voltage potential across the third fluid stream causes movement of at least a portion of at least one of the selected compound and selected biological contaminants remaining in the first fluid stream through the second selective membrane into the third fluid stream.

66. (New) The method according to claim 63 wherein the method further comprises directing a fourth fluid stream separated from the second fluid stream by a third selective membrane, wherein the preselected pore size of the third selective membrane allows selective migration of components in the second fluid stream through the third selective membrane into the fourth fluid stream.

67. (New) The method according to claim 66 wherein the third selective membrane has a preselected pore size so as to substantially prevent at least one of any biological contaminants removed to the second fluid stream and any other compounds in the second fluid stream from migrating through the third selective membrane into the fourth fluid stream and substantially retain the at least one of the selected biological contaminants and other components in the second fluid stream.

68. (New) The method according to claim 66 wherein the application of a voltage potential across the fourth fluid stream causes migration of at least a portion of at least one of any biological contaminants removed to the second fluid stream, and any other compounds in the second fluid stream through the third selective membrane into fourth fluid stream.

69. (New) The method according to claim 61 wherein the step of directing a third fluid stream directing the third fluid stream so as to be separated from the second fluid stream by the second selective membrane.

70. (New) The method according to claim 69 wherein the second selective membrane has a preselected pore size so as to substantially prevent at least one of any biological contaminants removed to the second fluid stream and any other compounds in the second fluid stream from migrating through the second selective membrane into the third fluid stream.

71. (New) The method according to claim 69 wherein the application of a voltage potential across the third fluid stream causes migration of at least a portion of at least one of any biological contaminants removed to the second fluid stream, and any other compounds in the second fluid stream through the second selective membrane into third fluid stream.

72. (New) The method according to claim 69 wherein the method further comprises directing a fourth fluid stream separated from the first fluid stream by a third selective membrane, wherein the preselected pore size of the third selective membrane allows selective migration of components in the first fluid stream through the third selective membrane into the fourth fluid stream.

73. (New) The method according to claim 72 wherein the third selective membrane has a preselected pore size so as to substantially prevent at least one of the selected compound and selected biological contaminants remaining in the first fluid stream from migrating through the third selective membrane into the fourth fluid stream and substantially retain at least one of the selected compound and selected biological contaminants in the first fluid stream.
74. (New) The method according to claim 72 wherein the application of a voltage potential across the fourth fluid stream causes movement of at least a portion of at least one of the selected compound and selected biological contaminants remaining in the first fluid stream through the third selective membrane into the fourth fluid stream.
75. (New) The method according to claim 61 wherein the method further comprises periodically stopping and reversing the voltage potential to cause movement of at least any compounds of the first fluid stream having entered the first selective membrane to move back into the first fluid stream and wherein substantially not causing any of the selected compound and biological contaminants that have entered the second fluid stream to re-enter the first fluid stream.
76. (New) The method according to claim 61 wherein the first fluid stream further includes a compound from which the selected compound is separated, wherein such compound is selected from the group consisting of blood proteins, immunoglobulins, recombinant proteins, and combinations thereof.
77. (New) The method according to claim 61 wherein the biological contaminant is selected from the group consisting of viruses, bacteria, prions, yeast, lipopolysaccharides, toxins, endotoxins, and combinations thereof.
78. (New) The method according to claim 61 wherein the pH of the first fluid stream is selected by selectively adding a buffer having the required pH and the pH is selected at one of

a pH lower than the isoelectric point of the compound, a pH about the isoelectric point of the compound, and a pH higher than the isoelectric point of the compound.

79. (New) A method for isolating at least a portion of a selected compound from a fluid stream, the method comprising:

- (a) directing a first fluid stream having a selected pH and including at least a selected compound so as to flow along a first selective membrane;
- (b) directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby;
- (c) directing a third fluid stream separated from one of the first and second fluid streams by a second selective membrane;
- (d) applying at least one voltage potential across at least the first and second fluid streams, wherein the application of such at least one voltage potential causes movement of at least a portion of the selected compound through the first selective membrane into the second fluid stream, wherein the second selective membrane has a preselected pore size that allows selective migration of components in at least one of the first and second fluid streams through the second selective membrane into the third fluid stream; and
- (e) maintaining step (d) until at least one of the fluid streams contains a desired purity of the selected compound.

80. (New) The method according to claim 79 wherein the first selective membrane has a preselected pore size so as to allow selective migration of components in the first fluid stream through the first selective membrane into the second fluid stream and selectively retain other components in the first fluid stream.

81. (New) The method according to claim 79 wherein the method further comprises directing a fourth fluid stream separated from the other of the first and second fluid streams by a third selective membrane, wherein the preselected pore size of the third selective membrane allows selective migration of components in the other of first and second fluid streams through the third selective membrane into the fourth fluid stream.

82. (New) A method for isolating at least a portion of a selected compound from a fluid stream, the method comprising:

- (a) directing a first fluid stream having a selected pH and including at least a selected compound so as to flow along a first selective membrane;
- (b) directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby;
- (c) directing a third fluid stream separated from one of the first and second fluid streams by a second selective membrane;
- (d) applying at least one voltage potential across at least the first and second fluid streams, wherein the application of such at least one voltage potential causes movement of at least a portion of components in the first fluid stream through the first selective membrane into the second fluid stream while the selected compound is prevented from entering the second fluid stream, wherein the second selective membrane has a preselected pore size that allows selective migration of components in at least one of the first and second fluid streams through the second selective membrane into the third fluid stream; and
- (e) maintaining step (d) until at least one of the fluid streams contains a desired purity of the selected compound.

83. (New) The method according to claim 82 wherein the first selective membrane has a preselected pore size so as to allow selective migration of components in the first fluid stream through the first selective membrane into the second fluid stream and selectively retain other components in the first fluid stream.

84. (New) The method according to claim 82 wherein the method further comprises directing a fourth fluid stream separated from the other of the first and second fluid streams by a third selective membrane, wherein the preselected pore size of the third selective membrane allows selective migration of components in the other of first and second fluid streams through the third selective membrane into the fourth fluid stream.

85. (New) A system for concurrently isolating at least a portion of both a selected compound and biological contaminants from a fluid stream, the system comprising:

means for directing a first fluid stream having a selected pH and including at least one biological contaminant and a selected compound so as to flow along a first selective membrane;

means for directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby;

means for directing a third fluid stream separated from one of the first and second fluid streams by a second selective membrane; and

means for applying at least one voltage potential across at least the first and second fluid streams, wherein the application of such at least one voltage potential causes movement of at least a portion of at least one of a selected compound and the biological contaminants through the first selective membrane into the second fluid stream, wherein the preselected pore size of the second selective membrane allows selective migration of components in at least one of the first and second fluid streams through the second selective membrane into the third fluid stream.

86. (New) A system for concurrently isolating at least a portion of both a selected compound and biological contaminants from a fluid stream, the system comprising:

means for directing a first fluid stream having a selected pH and including at least one biological contaminant and a selected compound so as to flow along a first selective membrane;

means for directing a second fluid stream along the first selective membrane so as to be isolated from the first fluid stream thereby;

means for directing a third fluid stream separated from one of the first and second fluid streams by a second selective membrane; and

means for applying at least one voltage potential across at least the first and second fluid streams, wherein the application of such at least one voltage potential causes movement of at least a portion of the biological contaminants through the first selective membrane into the second fluid stream while the selected compound is prevented from entering the second fluid stream, wherein the preselected pore size of the second



**selective membrane allows selective migration of components in at least one of the first and second fluid streams through the second selective membrane into the third fluid stream.**

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